

## Differentiation of Human Embryonic Stem Cells into Urothelium

### Grant Award Details

Differentiation of Human Embryonic Stem Cells into Urothelium

**Grant Type:** Basic Biology II

**Grant Number:** RB2-01567

**Project Objective:** PI has successfully derived Hg line into DE cells and differentiated them into urothelial cells of the bladder in the rodent model.

**Investigator:**

**Name:** Eric Kurzrock

**Institution:** University of California, Davis

**Type:** PI

**Disease Focus:** Pediatrics

**Human Stem Cell Use:** Embryonic Stem Cell

**Award Value:** \$849,037

**Status:** Closed

### Progress Reports

**Reporting Period:** Year 1

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**Reporting Period:** Year 2 + NCE

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### Grant Application Details

**Application Title:** Differentiation of Human Embryonic Stem Cells into Urothelium

**Public Abstract:**

Augmentation or replacement of the bladder is often necessary for the treatment of adults with bladder cancer and children with spinal cord injury or spina bifida. Current surgical techniques utilize segments of intestine or stomach as a substitute for bladder wall. Use of intestinal segments is associated with many complications including infection, stones, salt imbalance, and most concerning, cancer. An ideal substitute for bladder wall would be bioengineered bladder tissue. Ideally, a bioengineered graft would consist of cells that are genetically normal and free of cancerous mutations, promote blood vessel growth, survive long-term and regenerate. Stem cells appear to be the ideal solution for bioengineering tissue.

Preliminary clinical trials have demonstrated the feasibility of using bioengineered tissue for bladder augmentation. The bladder is lined by a very unique cell type called "urothelium". The ability to induce human embryonic stem cells (hESC) or induced pluripotent stem cells (iPSC) into urothelium would provide a major advancement in the tissue engineering field, scientifically and clinically. In addition, deciphering the mechanisms of hESC to urothelial differentiation would facilitate investigation of deviated differentiation into urothelial cancer stem cells; the "seeds" of bladder cancer.

Bladder cancer is the fourth most common type of cancer and caused 15,000 deaths last year. Treatment often requires removal of the bladder. Like other tumors, bladder cancer is believed to originate from the transformation of stem cells into cancer stem cells (CSCs). Potential markers of urothelial CSCs have been identified. Surprisingly, the scientific community has not yet addressed the study of normal human urothelial stem cells and differentiation of hESC to urothelium. The investigation of mechanisms and markers involved in the differentiation of hESC into urothelium will yield important facts about normal and abnormal differentiation and will ultimately help predict the malignancy of bladder cancers and improve treatments.

Our specific aims are to induce the differentiation of hESC into urothelium via cell signaling. We will also investigate the genes involved in this process. And, we will test the feasibility of transplanting hESC-derived urothelium into a bladder.

This investigation will lead to advances in stem cell biology in an important area not addressed by other scientists. The successful completion of this project will improve human health, indirectly through increased knowledge of differentiation pathways relevant to normal development and neoplasia, and directly through development of novel methodologies for bioengineering tissue for adults and children with urologic disorders and cancer. We are working in a very novel field, which has a high potential to save lives and to vastly improve the quality of life for many patients who need their bladder removed or enlarged.

**Statement of Benefit to  
California:**

The scientific community has not yet addressed the study of urothelial stem cells and differentiation of human embryonic stem cells (hESC) to urothelium. Our investigation of mechanisms and markers involved in the differentiation of hESC into urothelium will yield important facts about normal and abnormal differentiation and will help predict the malignancy of bladder cancers and improve treatments. This project will also advance the field of regenerative medicine. Adults with bladder cancer and children with spina bifida often need bladder reconstruction. Current surgical techniques use segments of intestine as a substitute for bladder wall. Use of intestinal segments is associated with many complications including cancer. Preliminary clinical trials have demonstrated the feasibility of using bioengineered tissue. The ability to induce hESC or induced pluripotent stem cells (iPSC) into urothelium would provide a major advancement in the regenerative medicine field, both scientifically and clinically.

Due to its high rate of recurrence, bladder cancer carries the highest lifetime cost to treat of all cancers. The successful completion of this project will improve human health, indirectly through increased knowledge of differentiation pathways relevant to normal bladder development and bladder cancer, and directly through development of novel methodologies for bioengineering tissue for adults and children with urologic disorders and cancer. These benefits will come to the citizens of California first. In addition to healthcare, this research will benefit the California economy by developing new protocols and technologies that could be adapted for other organs and tissues. Any health benefits, patents, new biotechnology or clinical trials would start in California. This research exemplifies the intent of CIRM bringing together clinical scientists with basic and translational scientists to develop stem cell treatments for the California public while at the same time advancing stem cell biology.

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